had been formed. The oxidation mixture showed in a 1.5-dm. tube an observed rotation of −2.90°. An equal quantity of authentic benzyl β-D-arabinopyranoside, similarly oxidized, gave a rotation of −2.95° while its anomer, benzyl α-D-arabinopyranoside, rotated +2.95°.

Benzyl β-D-Ribopyranoside Tribenzoate (IV) (a) from Benzyl β-D-Ribopyranoside.—Benzyl β-D-ribopyranoside (0.46 g.) was benzoylated with pyridine and benzoyl chloride in the usual manner to yield from 10 ml. of ethanol 1.00 g. (95%) of clear, square plates melting at 143–144°. Recrystallization from warm absolute alcohol gave material melting at 144–145° and rotating −108° in chloroform (*c* 1.28). In pure dioxane the substance rotated −110.5° (*c* 4.80).

Anal. Calcd. for $C_{33}H_{28}O_8$: C, 71.73; H, 5.11. Found: C, 71.83; H, 5.21.

(b) From Tri-*O*-benzoyl-β-D-ribopyranosyl Bromide (I).—Pure tri-*O*-benzoyl-β-D-ribopyranosyl bromide (3.64 g.) was shaken with 18 ml. of pure, anhydrous benzyl alcohol at room temperature until solution was complete. After 18 hours the reaction mixture was diluted with methylene dichloride, washed successively with aqueous sodium bicarbonate and water, and concentrated at 95° and 0.2 mm. pressure. From *ca.* 10 ml. of absolute ethanol the colorless residue deposited 1.87 g. (49%) of crystalline material which melted at 143–144° either alone or in admixture with the benzyl β-D-ribopyranoside tribenzoate prepared in (a) above.

Hydrogenolysis of Benzyl β-D-Ribopyranoside Tribenzoate (IV).—Two grams of palladium black was suspended in 25.0 ml. of pure dioxane in a 1.5-dm. polarimeter tube and saturated with hydrogen at room temperature. Benzyl β-D-ribopyranoside tribenzoate (1.0027 g.) was then added and the suspension shaken with hydrogen. After 19 minutes the theoretical quantity of hydrogen had been absorbed and the solution, read over the settled catalyst, showed a rotation of −2.13°, corresponding to a specific rotation (based on the theoretical yield of tri-*O*-benzoylpentose) of −42.3°. The solution showed a slow dextromutarotation on standing. After removal of the catalyst and solvent there was obtained from aqueous alcohol 0.61 g. (73%) of 2,3,4-tri-*O*-benzoyl-β-D-ribose melting at 134–135°. Mixed with authentic material it melted at 136–137°. The product showed a rotation of −43.3° in chloroform (*c* 1.09).

Tri-*O*-benzoyl-β-D-ribopyranosyl Bromide (I) from 2,3,4-Tri-*O*-benzoyl-D-ribose.—Each of the three forms of 2,3,4-tri-*O*-benzoyl-D-ribose (the pure β-isomer, the impure, dextrorotatory α-isomer and the prismatic form) gave the same yield in this preparation. In a typical experiment 5.00 g. of impure 2,3,4-tri-*O*-benzoyl-α-D-ribose ($[\alpha]^{20}\text{D}$ +4.9° in chloroform) was dissolved in a mixture of 10 ml. of ethylene dichloride, 10 ml. of hydrogen bromide in glacial acetic acid (32% HBr) and 4 ml. of acetic anhydride. After 2.5 hours at room temperature a mixture of 30 ml. of toluene and 5 ml. of acetic anhydride was added and the solution concentrated *in vacuo* (40–45° bath) to a thin sirup which crystallized spontaneously. Ether (20 ml.) was added, the mixture cooled to −5° and then 20 ml. of pentane added as crystallization proceeded. The mixture of prisms and needles thus obtained (4.58 g., 81%) melted at 152–154° (dec., rapid heating) and rotated −178.8° in absolute chloroform (*c* 1.96). Recrystallization from 10 ml. of methylene dichloride and 10 ml. of pentane gave 2.51 g. of pure tri-*O*-benzoyl-β-D-ribopyranosyl bromide melting at 155–158° (dec.) and rotating −203° in absolute chloroform (*c* 2.25).

Acknowledgment.—The analytical data were obtained by the Institute's Microanalytical Laboratory under the direction of Dr. William C. Alford.

BETHESDA, MARYLAND

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH, U. S. PUBLIC HEALTH SERVICE, DEPARTMENT OF HEALTH, EDUCATION AND WELFARE]

New Benzoyl Derivatives of D-Ribofuranose and *aldehydo*-D-Ribose. The Preparation of Crystalline 2,3,5-Tri-*O*-benzoyl-β-D-ribose from D-Ribose[1]

BY ROBERT K. NESS, HARRY W. DIEHL AND HEWITT G. FLETCHER, JR.

RECEIVED AUGUST 20, 1953

A method for the preparation of crystalline 2,3,5-tri-*O*-benzoyl-β-D-ribose from D-ribose in relatively high yield and without the isolation of intermediates is described. The structure of the new tribenzoate is demonstrated by its synthesis through the hydrogenolysis of benzyl β-D-ribofuranoside tribenzoate. Its anomeric configuration is assigned on the basis of methylation studies and on comparisons between its optical rotation and those of various closely related compounds. Acetylation of 2,3,5-tri-*O*-benzoyl-β-D-ribose affords crystalline 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribose; benzoylation gives β-D-ribofuranose tetrabenzoate which may also be prepared through the benzoylation of D-ribose in pyridine at an elevated temperature. The possible utility of 2,3,5-tri-*O*-benzoyl-β-D-ribose as a stable precursor for the synthesis of D-ribofuranosides is investigated through its use for the preparation of benzyl β-D-ribofuranoside tribenzoate. A second new D-ribose tetrabenzoate, *aldehydo*-D-ribose tetrabenzoate, has been prepared in crystalline form for comparison purposes.

In a recent paper[2] there has been described a procedure whereby the α- and β-D-xylofuranose tetrabenzoates may be prepared from D-xylose without the isolation of intermediates. In this procedure D-xylose is dissolved in methanol containing 1% of hydrogen chloride and the reaction halted when the yield of methyl D-xylofuranosides has reached a maximum. The amorphous mixture thus obtained is benzoylated in normal fashion and the mixture of benzoates treated with hydrogen bromide in glacial acetic acid. The benzoylated D-xylofuranosyl and D-xylopyranosyl bromides thus formed are then hydrolyzed and the pyranose portion very largely eliminated through the crystallization of 2,3,4-tri-*O*-benzoyl-α-D-xylose which is, indeed, the main product of these reactions. In the mother liquor the remaining amorphous 2,3,5-tri-*O*-benzoyl-D-xylose is benzoylated to give the crystalline, anomeric tetrabenzoates of D-xylofuranose in a total over-all yield of 33%. Application of this synthetic process to the D-ribose series has led to very different results which will now be described.

It is well known that while crystalline D-ribose exists in the pyranose form,[3] it appears to assume the furanose form with greater ease than the majority of sugars and, indeed, occurs in nature largely, if not wholly, as furanose derivatives.[4] In view of

---

(1) A preliminary account of this work appeared in THIS JOURNAL, **75**, 3289 (1953).

(2) H. G. Fletcher, Jr., *ibid.*, **75**, 2624 (1953).

(3) R. Jeanloz, H. G. Fletcher, Jr., and C. S. Hudson, *ibid.*, **70**, 4052 (1948).

(4) See R. W. Jeanloz and H. G. Fletcher, Jr. [*Advances in Carbohydrate Chem.*, **6**, 135 (1951)] for a recent review of ribose chemistry.

this it is not surprising that D-ribose behaves quite differently in the above-described sequence of reactions than does D-xylose. As was observed by Levene, Raymond and Dillon,[5] D-ribose loses its reducing power in dilute methanolic hydrogen chloride more rapidly than does D-xylose. Furthermore, later on in the sequence of reactions, at the tribenzoate state, no 2,3,4-tri-*O*-benzoyl-β-D-ribose[6] (a readily crystallized substance) could be isolated. Instead there was obtained from aqueous pyridine solution a tri-*O*-benzoylpentose which crystallized with pyridine, but could thereafter readily be obtained in crystalline, solvent-free form, the yield of this latter varying from 70 to 81% based on the D-ribose used.

The structure of this new tribenzoate was demonstrated in a variety of ways. The first method involved an alternative, less equivocal synthesis from D-ribose. The sugar was treated with benzyl alcohol containing 1% of hydrogen chloride and, as soon as the reducing power was no longer detectable with Fehling solution, acid was removed and there was obtained a crystalline benzyl D-riboside which consumed but one mole of periodate. The product of the oxidation showed the same rotation as that made similarly from an equivalent quantity of benzyl β-D-glucopyranoside, a substance whose anomeric configuration has been adequately proved.[7] These facts demonstrate that the new glycoside is benzyl β-D-ribofuranoside. Its tribenzoate was found to be readily crystalline[8] and, on catalytic hydrogenolysis,[9] afforded the previously obtained D-ribose tribenzoate in good yield. The compound may then be assigned the structure 2,3,5-tri-*O*-benzoyl-D-ribose.[9a]

The evidence for the anomeric configuration of the crystalline 2,3,5-tri-*O*-benzoyl-D-ribose rests upon somewhat less certain grounds. The substance mutarotates rapidly but very slightly to the right in acidic aqueous dioxane and slowly (but also very slightly) to the left in chloroform. These changes are conflicting and of such a small magnitude that no definite conclusion regarding the anomeric configuration can be drawn from them.[10]

Methylation of the tribenzoate followed by catalytic debenzoylation afforded an amorphous mixture of methyl D-ribofuranosides which, as expected, consumed one molar equivalent of periodate. Comparison of the rotation of the dialdehyde produced by the oxidation with the rotations of the dialdehydes similarly formed from methyl α-D-mannopyranoside and methyl β-D-galactopyranoside indicated that the methyl D-ribofuranoside consisted of 80.6% β-anomer and 19.4% α-anomer. This evidence favors the β-configuration for 2,3,5-tri-*O*-benzoyl-D-ribose.

When the tribenzoate is acetylated at low temperature in pyridine solution it is converted in high yield to 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-D-ribose.[10a] Benzoylation under similar conditions affords a D-ribose tetrabenzoate, a substance which could also be obtained by the direct benzoylation of D-ribose in pyridine solution at 100°.[11,11a]

This D-ribose tetrabenzoate was not identical with the known β-D-ribopyranose tetrabenzoate[3] nor with *aldehydo*-D-ribose tetrabenzoate which was synthesized for comparison purposes by successive benzoylation and demercaptalation of the *aldehydo*-D-ribose diisobutyl thioacetal of Zinner.[12] It is apparent, then, that the new tetrabenzoate and new 1-*O*-acetate are derivatives of D-ribofuranose.[13] From the mode of preparation and the high yields obtained it may safely be assumed that the anomeric configurations of the acetate and the tetrabenzoate are the same as that of crystalline 2,3,5-tri-*O*-benzoyl-D-ribose.

The molecular rotations of some of the above-mentioned substances with the analogous benzoylated derivatives of D-ribopyranose may be compared in Table I. The anomeric configurations of the pyranose derivatives have been established through previous work[3,6] while the anomeric configuration of benzyl β-D-ribofuranoside tribenzoate was unequivocably fixed as described above. Inspection of the molecular rotations shows that the order of these substances according to increasing molecular dextrorotation is the same in both series, *i.e.*, benzyl pentoside tribenzoate < pentose tetra-

---

(5) P. A. Levene, A. L. Raymond and R. T. Dillon, *J. Biol. Chem.*, **95**, 699 (1932).

(6) H. G. Fletcher, Jr., and R. K. Ness, THIS JOURNAL, **76**, 760 (1954).

(7) E. Fischer and B. Helferich, *Ann.*, **383**, 68 (1911).

(8) The yield of crystalline benzyl β-D-ribofuranoside from D-ribose directly was found the same as that which can be obtained indirectly through the benzoylation of crude, amorphous benzyl β-D-ribofuranoside and catalytic debenzoylation of the resulting crystalline tribenzoate.

(9) Unfortunately the rate of hydrogenolysis under the conditions tried was too slow to allow conclusions regarding the anomeric configuration of the product as was possible in a parallel case in the D-ribopyranose series (ref. 6).

(9a) The physical constants of this substance exclude the possibility that it is identical with the compound given this designation by F. Weygand and F. Wirth [*Chem. Ber.*, **85**, 1000 (1952)]. In a paper which will appear shortly we will discuss the structure of the product described by these authors.

(10) We speculated that the slow levomutarotation of the 2,3,5-tri-*O*-benzoyl-D-ribose in chloroform might be due to equilibration with a less strongly rotatory aldehydo form. The strong ultraviolet absorption of the three ester carbonyls in the substance precluded the detection of an aldehydo group. Comparison of the infrared spectra of fresh and mutarotated chloroform solutions showed only that there was a slightly larger amount of hydrogen bonding in the latter. Inspection of models appears to indicate that somewhat more hydrogen bonding is to be expected in 2,3,5-tri-*O*-benzoyl-*aldehydo*-D-ribose than in either of the anomeric cyclic tautomers.

(10a) Weygand and Wirth (ref. 9a) as well as F. Weygand and W. Sigmund [*Chem. Ber.*, **86**, (1953)] have obtained this substance from several nucleosides by a series of reactions. We are indebted to Prof. Weygand for confirming the fact that his material is identical with ours.

(11) The physical constants which we obtained for this substance indicate that it is identical with the β-D-ribofuranose tetrabenzoate reported by Weygand and Wirth (ref. 9a).

(11a) The high temperature acylation of sugars to obtain furanose derivatives appears to have been introduced as a preparative method by H. H. Schlubach and V. Prochownick [*Ber.*, **62**, 1502 (1929); *ibid.*, **63**, 2298 (1930); see also R. K. Ness, H. G. Fletcher, Jr., and C. S. Hudson, THIS JOURNAL, **73**, 3742 (1951)], and one of us (ref. 2) has recently used it to prepare the anomeric tetrabenzoates of D-xylofuranose. H. Zinner [*Chem. Ber.*, **83**, 153 (1950)] has studied the acetylation of D-ribose at elevated temperatures and has found that both β-D-ribopyranose and β-D-ribofuranose tetraacetates are formed—a mixture which is somewhat difficult to separate by fractional crystallization (private communication from Dr. B. R. Baker). We have now found that the benzoylation of D-ribose in hot pyridine solution gives similar results, both β-D-ribopyranose and β-D-ribofuranose tetrabenzoates being formed, and here also the fractionation of the crystalline mixture is both laborious and wasteful.

(12) H. Zinner, *Chem. Ber.*, **83**, 275 (1950).

(13) Treatment with hydrogen bromide in glacial acetic acid followed by hydrolysis and then crystallization from aqueous pyridine converted both of these esters back to the original 2,3,5-tri-*O*-benzoyl-D-ribose.

TABLE I

BENZOYLATED DERIVATIVES OF D-RIBOSE

	$[\alpha]^{20}\text{D}$ (CHCl$_3$)	$[M]^{20}\text{D}$
Benzyl β-D-ribopyranoside tribenzoate	−108°[a]	−59,700
β-D-Ribopyranose tetrabenzoate	−102°[b]	−57,800
2,3,4-Tri-*O*-benzoyl-β-D-ribose	−42.2°[a]	−19,500
Benzyl β-D-ribofuranoside tribenzoate	+ 14.9°	+ 8,240
β-D-Ribofuranose tetrabenzoate	+ 17.0°	+ 9,640
2,3,5-Tri-*O*-benzoyl-β-D-ribose	+ 68.8°	+31,800

[a] Ref. 6. [b] Ref. 3.

benzoate < pentose tribenzoate. On the quantitative side, examination of Table II shows that molecular differences among the three compounds in the two series are of the same order of magnitude; that the actual numerical values do not agree closely is hardly surprising when it is recalled that we are comparing substances of different ring structures. In any event the values are such as to preclude with considerable certainty the possibility that any of the substances is an α-isomer and we deem these considerations of molecular rotation as providing strong evidence in favor of the assignment of the β-configuration to 2,3,5-tri-*O*-benzoyl-D-ribose, D-ribofuranose tetrabenzoate and 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-D-ribose.

TABLE II

DIFFERENCES AMONG MOLECULAR ROTATIONS OF BENZOYLATED D-RIBOSE DERIVATIVES

	Ribopyranose series	Ribofuranose series
Pentose tetrabenzoate–pentose tribenzoate	+38,300	+22,160
Pentose tetrabenzoate–benzyl pentoside tribenzoate	− 1,900	− 1,400
Pentose tribenzoate–benzyl pentoside tribenzoate	−40,200	−23,560

The preparation of 2,3,5-tri-*O*-benzoyl-β-D-ribose, a stable, crystalline D-ribofuranose derivative, in relatively high yield directly from D-ribose without the isolation of intermediates may have some utility as a step in an improved path in the synthesis of D-ribofuranosides. We have explored this possibility through the synthesis of benzyl β-D-ribofuranoside from 2,3,5-tri-*O*-benzoyl-β-D-ribose. When this latter compound was treated with a mixture of hydrogen bromide, glacial acetic acid and acetic anhydride tri-*O*-benzoyl-D-ribofuranosyl bromide[14,15] was obtained in amorphous form. Upon reaction with benzyl alcohol *in the absence of an acid acceptor* the bromide afforded pure benzyl β-D-ribofuranoside tribenzoate in 54% yield, identical with the substance prepared earlier. The value of 2,3,5-tri-*O*-benzoyl-β-D-ribose as a precursor for the synthesis of other D-ribofuranosides is being studied further.

In passing we wish to observe that the use of pyridine for the crystallization of the hydrolysis product of tri-*O*-benzoyl-D-ribofuranosyl bromide is essential since a major product of the reaction is an isomer of the desired 2,3,5-tri-*O*-benzoyl-β-D-ribose. This isomer, which will be the subject of a paper to be published in the near future, is converted into 2,3,5-tri-*O*-benzoyl-β-D-ribose through the action of pyridine.

Crystalline ribitol pentabenzoate, prepared in the course of these studies, is described.

Experimental[16]

2,3,5-Tri-*O*-benzoyl-β-D-ribose from D-Ribose.—Five grams of pure, powdered D-ribose ($[\alpha]^{20}\text{D}$ −20°, equilibrium in H_2O) was added to 120 ml. of methanol containing 1% of hydrogen chloride (0.216 *N*)[17] and the mixture stirred until solution was complete. After approximately 45 minutes at room temperature (27°) test of a sample of the mixture with Fehling solution showed that the reducing power had almost disappeared[18] and 6 ml. of pyridine was then added. The reaction mixture was concentrated *in vacuo* at 30–35° to a stiff sirup which was dissolved in 50 ml. of pyridine and the resulting solution, after cooling, treated with 14 ml. of benzoyl chloride. After the reaction was largely complete, the mixture was held at 40° for 1.5 hr., cooled and treated with a chip of ice to decompose the excess of benzoyl chloride. The reaction mixture was then diluted with methylene dichloride and washed successively with cold water, cold 3 *N* sulfuric acid and aqueous sodium bicarbonate, moisture finally being removed with sodium sulfate. The solution was filtered through carbon and concentrated *in vacuo* (35–40° bath) to a heavy sirup which was diluted with 32 ml. of dry methylene dichloride and the solution cooled to 20°. Hydrogen bromide in glacial acetic acid (32 ml., 32% HBr) was added and after 20 min. at 20°, when mutarotation had ceased, the reaction mixture was washed successively with cold water and aqueous sodium bicarbonate and then poured into a vigorously stirred mixture of 90 ml. of acetone, 2 ml. of water and 5 g. of silver carbonate. Stirring was continued for 0.5 hr., the solids were removed by filtration through carbon and the solvent was removed *in vacuo* at 45° to give a heavy sirup. This latter was dissolved in 120 ml. of pyridine, the solution cooled to 0°, and 75 ml. of water added. After standing at −5° the product crystallized with pyridine of crystallization; m.p. *ca.* 62–65°. The solvent of crystallization was readily lost and attempts to obtain the solvated material in reproducible form failed. Analytical data indicated that the crystalline addition compound contained somewhat more than one-half mole of pyridine. The pyridine addition compound, washed well with a mixture of 4:3 pyridine–water at −5°, was dried *in vacuo* over sulfuric acid and sodium hydroxide at room temperature. The product (12.9 g.) together with a small second crop (1.1 g.) was dissolved in 14 ml. of absolute alcohol, the solution cooled to 0°, seeded with the anhydrous form and kept cool, until a crystalline magma was obtained. Dried *in vacuo* over sulfuric acid and sodium hydroxide the product (12.5 g., 81%) consisted of nearly pure 2,3,5-tri-*O*-benzoyl-β-D-ribose melting at 102–104° and rotating +69.0° in chloroform. The substance could conveniently be re-

---

(14) As was pointed out in a previous paper (ref. 6), dealing with parallel compounds of the D-ribopyranose series, the tri-*O*-benzoyl-D-ribose is much more suitable for the preparation of the bromide than is the corresponding D-ribose tetrabenzoate since, in the latter case, hydrogen bromide cleaves benzoic acid from carbon one and this by-product can only be removed by subjecting the mixture to extraction with aqueous sodium bicarbonate, an undesirable procedure in view of the ease of hydrolysis of the bromide.

(15) Evidence that this bromide is, at least in large part, the β-anomer will be adduced in a later paper.

(16) Melting points cited are corrected. Rotations are specific rotations for the D-line of sodium at 20°, concentration being expressed in g. per 100 ml. of solution.

(17) Even at room temperature dry methanol reacts with hydrogen chloride [*cf.* S. R. Carter and J. A. V. Butler, *J. Chem. Soc.*, **125**, 963 (1924)] to form methyl chloride and water. For this reason the methanolic hydrogen chloride used here should be freshly prepared and recently titrated.

(18) Since the rate of reaction is affected by the concentration of the acid and by the temperature it is advisable to carry out identical Fehling tests at five-minute intervals. Inspection of a series of such tests will greatly facilitate the choice of a point to halt the reaction. We have standardized the Fehling test for this preparation as follows: 0.1 ml. of reaction mixture is mixed with 5 drops of each of the Fehling solutions and heated at 100° for exactly one minute.

crystallized from alcohol–pentane, ether–pentane or carbon tetrachloride and when pure melted at 111–112° although this value was not sharp and varied somewhat from sample to sample and with the rate of heating. In U.S.P. chloroform (*c* 2.0) the compound mutarotated +68.8 → 66.2° in 2 days; in absolute chloroform (*c* 6.0) it mutarotated +67.7 → 65.6° in 2 days. In 18:7 dioxane–water (v./v.) (*c* 2.07) it rotated +67.4°; when an approximately equimolar quantity of hydrogen bromide was added the rotation increased, becoming constant at +68.1° in 15 minutes.

Anal. Calcd. for $C_{26}H_{22}O_8$: C, 67.52; H, 4.80. Found: C, 67.31; H, 4.91.

Benzyl β-D-Ribofuranoside Tribenzoate (a) from D-Ribose.—Five grams of pure, powdered D-ribose was added to 150 ml. of benzyl alcohol containing 1% of hydrogen chloride and the mixture stirred at room temperature. At the end of 40 minutes the reducing power of the solution was no longer detectable with Fehling solution and after 45 minutes 9.0 g. of silver carbonate was added. The mixture was stirred an additional 10 minutes and then filtered through a thin layer of carbon. Benzyl alcohol was removed from the filtrate by distillation at *ca.* 0.5 mm. and 85–90° (bath). The residual sirup (8.3 g.) was dissolved in 50 ml. of pyridine and, with cooling, 15 ml. of benzoyl chloride was added. After being heated at 40° for one hour the reaction mixture was diluted with ethylene dichloride and washed successively with cold water, cold 3 *N* sulfuric acid and aqueous sodium bicarbonate. Moisture was removed with sodium sulfate and the solution concentrated *in vacuo* to a sirup which, from 45 ml. of ether at −5°, gave 9.6 g. (52%) of needles melting at 60–66° and rotating +13.6° in chloroform. Recrystallized from 10 parts of absolute alcohol, the product was obtained in pure form melting at 87–88° and rotating +14.9° in chloroform (*c* 0.81).

Anal. Calcd. for $C_{32}H_{28}O_8$: C, 71.73; H, 5.11. Found: C, 71.58; H, 5.25.

(b) From 2,3,5-Tri-*O*-benzoyl-β-D-ribose.—A solution of 1.00 g. of 2,3,5-tri-*O*-benzoyl-β-D-ribofuranose in a mixture of 2.7 ml. of ethylene dichloride, 0.27 ml. of acetic anhydride and 2.7 ml. of hydrogen bromide–glacial acetic acid (32% HBr) was allowed to stand at room temperature for 1.5 hours. Methylene dichloride was then added and the reaction mixture was washed with cold aqueous sodium bicarbonate.[19] After drying the organic layer with Drierite and filtering with carbon, the solvent was removed under reduced pressure (35°) leaving a clear, colorless sirup. Anhydrous benzyl alcohol (0.80 ml.) was added; within one minute the solution became yellow. After 25 min. spontaneous crystallization occurred and after 75 min. 5 ml. of absolute alcohol and 10 ml. of pentane were added and the crystals formed removed by filtration: 0.91 g., m.p. 68–73°. After three recrystallizations from absolute alcohol, 0.65 g. (55%) of pure benzyl β-D-ribofuranoside tribenzoate melting at 86–87° was obtained. Admixture with authentic material prepared in (a) above did not lower the melting point.

Benzyl β-D-Ribofuranoside. (a) From Benzyl β-D-Ribofuranoside Tribenzoate.—The benzyl β-D-ribofuranoside tribenzoate (6.4 g.) was suspended in 25 ml. of absolute methanol and treated with 3 ml. of 1 *N* barium methoxide. The compound dissolved in 15 minutes; after 2 days at room temperature barium was removed by passage of the solution through a column (2.5 × 18.0 cm.) of Amberlite IR-120.[20] The solution was then concentrated *in vacuo* (40° bath) to a crystalline mass. From 10 ml. of ethyl acetate there was obtained 2.05 g. (74%) of needles melting at 92–96°. Recrystallized from 10 ml. of ethyl acetate these melted at 95–96° and rotated −60.5° in water (*c* 0.73).

Anal. Calcd. for $C_{12}H_{16}O_5$: C, 59.99; H, 6.71. Found: C, 60.00; H, 6.68.

A sample (123.7 mg., 0.000515 mole) of the benzyl β-D-ribofuranoside was oxidized with sodium metaperiodate using the technique of Jackson and Hudson.[21] After 17 hours the compound was found to have consumed 0.95 molar equivalent of oxidant and showed in a 1.5-dm. tube an observed rotation of −0.87°. In a parallel experiment benzyl β-D-glucopyranoside (139.2 mg., 0.000515 mole) consumed 1.97 molar equivalents of oxidant with the concomitant formation of 0.95 mole of formic acid to give a solution showing an observed rotation in a 1.5-dm. tube of −0.87°.

(b) From D-Ribose.—Crude, sirupy benzyl β-D-ribofuranoside was prepared from 5 g. of D-ribose as described above for the preparation of its tribenzoate. Dissolved in 35 ml. of ethyl acetate and seeded this gave 3.07 g. (38%) of product melting at 94–96° and rotating −60.0° in water. Recrystallized from 5 parts of ethyl acetate it rotated −60.2° in water (*c* 0.71) and melted at 95–96° either alone or in admixture with benzyl β-D-ribofuranoside prepared in (a) above.

2,3,5-Tri-*O*-benzoyl-β-D-ribose from Benzyl β-D-Ribofuranoside Tribenzoate.—Palladium chloride on carbon[22] (0.72 g.), suspended in ethyl acetate, was reduced with hydrogen at room temperature and atmospheric pressure. The activated catalyst was filtered, washed with ethyl acetate and added to a solution of 2.002 g. of benzyl β-D-ribofuranoside tribenzoate in 14 ml. of ethyl acetate. The suspension was then shaken with hydrogen at room temperature and pressure for 17.5 hr. After removal of the catalyst the solution (which gave a strongly positive Fehling test) was concentrated *in vacuo* to a stiff sirup. From 5 ml. of ether and 6 ml. of pentane there was obtained 0.60 g. (36%) of product melting at 102–105°. Mixed with 2,3,5-tri-*O*-benzoyl-β-D-ribose prepared directly from D-ribose the product melted at 102–105°.

Methylation of 2,3,5-Tri-*O*-benzoyl-β-D-ribose.—A solution of 2,3,5-tri-*O*-benzoyl-β-D-ribose (2.00 g.) in methyl iodide (10.0 ml.) was shaken with silver oxide (1.0 g.) and powdered Drierite at room temperature. After four days, the solids were removed by filtration and the filtrate concentrated *in vacuo*. Three batches of methylene dichloride were successively distilled from the sirup which was finally debenzoylated in 25 ml. of methanol with 2 ml. of 1.5 *N* barium methoxide. The reaction mixture, diluted with water, was deionized by passage through a column of Amberlite IR-120,[20] partially concentrated *in vacuo* and then extracted four times with chloroform to remove methyl benzoate. Concentration *in vacuo* gave a stiff sirup. Oxidation of 0.1394 g. of this sirup in 25 ml. of water with sodium metaperiodate by the procedure of Jackson and Hudson[21] required, after 26 hours, 1.02 moles of oxidant, afforded 0.10 mole of acid and showed, after one day, a constant rotation of −0.71° in a 1.5-dm. tube corresponding to a specific rotation of −94° for the dialdehyde formed. Under similar conditions, 0.1394 g. of methyl α,D-mannopyranoside and 0.1384 g. of methyl β-D-galactopyranoside yielded specific rotations of +126° and −147°, respectively, for the dialdehydes produced.

β-D-Ribofuranose Tetrabenzoate. (a) From D-Ribose.—Fifty grams of D-ribose was dissolved in 500 ml. of anhydrous pyridine and the solution held at 100° for one minute. While the reaction flask was cooled with an air blast, 190 ml. of benzoyl chloride was added at such a rate that the temperature of the rapidly stirred mixture remained at 98–102°. When the mixture had cooled to 35°, 500 ml. of chloroform was added and the solution washed successively with cold water, 3 *N* sulfuric acid and aqueous sodium bicarbonate. Moisture was removed with sodium sulfate, the solution filtered through carbon and concentrated *in vacuo* (50° bath) to a stiff, dark-brown sirup which was dissolved in 250 ml. of absolute ethanol and reconcentrated *in vacuo*. From its solution in 3 l. of absolute ethanol there was deposited 63.5 g. (34%) of crystalline material melting at 109–119° and showing −28.9° in chloroform.[23] Recrystallized from 10 parts of absolute ethanol at 50° this crude product yielded 20.8 g. (11%) of elongated prisms melting at 120–122°. Another recrystallization from 10 parts of absolute ethanol gave, with negligible loss, material melting at 121–122°; further recrystallization failed to alter this melting

---

[19] This preparation would be simplified and the yield probably improved were the excess reactants removed through codistillation *in vacuo* with toluene rather than by washing with aqueous alkali. See ref. 6.

[20] Product of Rohm and Haas Co., Philadelphia, Pa.

[21] E. L. Jackson and C. S. Hudson, This Journal, 59, 994 (1937).

[22] R. Mozingo, *Org. Syntheses*, **26**, 77 (1946): method C.

[23] This rotation corresponds to a mixture consisting of 61.3% of β-D-ribofuranose tetrabenzoate and 38.7% β-D-ribopyranose tetrabenzoate. On this basis the yield of furanose tetrabenzoate is 21%—a yield never actually obtained because of the difficulty in separating the mixture efficiently. Benzoylations conducted at 100° gave yields of furanose tetrabenzoate (calculated as above) ranging from 21 to 27%. Benzoylations at 110 and 115° gave yields of 26 and 28%, respectively.

point. The pure β-D-ribofuranose tetrabenzoate showed in chloroform (*c* 0.84) a rotation of +17.0°.

Anal. Calcd. for $C_{33}H_{26}O_9$: C, 69.96; H, 4.63. Found: C, 70.12; H, 4.82.

(b) **From 2,3,5-Tri-*O*-benzoyl-β-D-ribose.**—One gram of 2,3,5-tri-*O*-benzoyl-β-D-ribose was added to a mixture of 6 ml. of pyridine and 1 ml. of benzoyl chloride which had previously been chilled in ice. After solution was complete at 0° the mixture was slowly warmed, finally being heated at 40 for 1.5 hr. Ice and methylene dichloride were then added to the cooled solution, and the organic layer washed successively with water, 3 *N* sulfuric acid and aqueous sodium bicarbonate. Water was removed with sodium sulfate and the solution concentrated *in vacuo* to a stiff sirup which, from 7 ml. of absolute alcohol, gave 1.0949 g. (89%) of crystalline product rotating +17° (*c* 1.34, $CHCl_3$) and melting at 120–121° either alone or in admixture with pure β-D-ribofuranose tetrabenzoate prepared in (a) above.

1-*O*-Acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribose.—One gram of 2,3,5-tri-*O*-benzoyl-β-D-ribofuranose was added to a mixture of 5 ml. of pyridine and 2 ml. of acetic anhydride which had previously been cooled in an ice-bath. When solution was complete the mixture was held at room temperature for 15 min. and then at 40° for 1 hr. Ice-water and methylene dichloride were added to the cooled solution and the organic layer washed successively with water, 3 *N* sulfuric acid and aqueous sodium bicarbonate. Moisture was removed with sodium sulfate and the clear, colorless solution concentrated to a stiff sirup which, from 11 ml. of absolute alcohol, gave 964.9 mg. (88%) of micaceous plates melting at 130–131°. Recrystallization from 40 parts of alcohol gave, with negligible loss, material of the same melting point which rotated +44.2° in chloroform (*c* 1.32).

Anal. Calcd. for $C_{28}H_{24}O_9$: C, 66.66; H, 4.80. Found: C, 66.58; H, 4.92.

Ribitol Pentabenzoate.—Two grams of ribitol was suspended in 40 ml. of pyridine and treated with 10 ml. of benzoyl chloride and the reaction mixture warmed to 50°. The cooled mixture was then poured on ice and the gum thus precipitated dissolved in 90 ml. of absolute alcohol to give 7.6 g. (86%) of product melting at 97–101°. Recrystallized from 14 parts of absolute ethanol the ribitol pentabenzoate was obtained as prisms which melted at 108–109°; further recrystallization failed to change this melting point.

Anal. Calcd. for $C_{40}H_{32}O_{10}$: C, 71.42; H, 4.80. Found: C, 71.57; H, 5.02.

Tetra-*O*-benzoyl-*aldehydo*-D-ribose Diisobutyl Thioacetal.—Two grams of *aldehydo*-D-ribose diisobutyl thioacetal prepared by the method of Zinner[12] was benzoylated with pyridine and benzoyl chloride in the usual fashion. The product crystallized spontaneously when the reaction mixture was poured on ice. Recrystallized from 10 parts of methanol the pure material was obtained as prisms (4.2 g., 90%) melting at 108–109°. Further recrystallization failed to change this melting point. The tetra-*O*-benzoyl-*aldehydo*-D-ribose diisobutyl thioacetal showed a rotation of +8.5° in chloroform (*c* 0.86).

Anal. Calcd. for $C_{41}H_{44}O_8S_2$: C, 67.56; H, 6.08; S, 8.80. Found: C, 67.61; H, 6.11; S, 8.71.

***aldehydo*-D-Ribose Tetrabenzoate.**—To a solution of 3.8 g. of mercuric chloride in 10 ml. of acetone was added a solution of 1.8 g. of tetra-*O*-benzoyl-*aldehydo*-D-ribose diisobutyl thioacetal in 12 ml. of acetone. Water (8 ml.) was added and the reaction mixture heated at 60° for 1 hr. and at 40° overnight. The micaceous mercury compound which had formed was removed by filtration. The filtrate crystallized spontaneously yielding 0.60 g. of crude, unreacted starting material. The mother liquor was then concentrated to a small volume. Methylene dichloride was added and the organic layer washed with 10% aqueous potassium iodide, water and finally aqueous silver nitrate for removal of some free mercaptan. After drying with sodium sulfate and concentrating under reduced pressure at room temperature, the sirupy residue was dissolved in ether, the solution treated with decolorizing carbon and concentrated to a volume of *ca.* 5 ml. Pentane was added just below clouding at 0° and 1 hr. later crystallization was observed. The material (0.53 g., 57% corrected for recovered starting material) melted at 111–113° and gave a positive test with hot Fehling solution after 5 min. After a recrystallization from ether, the melting point became 112–113°. In absolute chloroform (*c* 0.81) it rotated −22°. In U.S.P. chloroform (*c* 1.39) it showed a rotation −26° after 3 min. and +2.7° after 16 hr. (not yet at equilibrium) and in 9:1 absolute ethanol-ethylene dichloride (*c* 0.95) of +52° (10 min.), +58° (31 hr.) and +64° (8 and 35 days).

Anal. Calcd. for $C_{33}H_{26}O_9$: C, 69.96; H, 4.63. Found: C, 70.24; H, 4.88.

Tetra-*O*-benzoyl-*aldehydo*-D-ribose 2,4-Dinitrophenylhydrazone.—The procedure of Neuberg, Grauer and Pisha[24] was used. To a solution of 318.5 mg. of *aldehydo*-D-ribose tetrabenzoate in 5 ml. of absolute ethanol was added a solution of 120 mg. of 2,4-dinitrophenylhydrazine in 10 ml. of 15% perchloric acid. The bright yellow precipitate (369 mg., 88%), which formed within a few minutes, melted at 80–95°. Recrystallized from a mixture of 1 ml. of methylene dichloride and 1.4 ml. of pentane the product was obtained as a mixture of rosettes of yellow needles and stout orange prisms. Separated mechanically, the prismatic form melted at 166–167°.

Anal. Calcd. for $C_{39}H_{30}O_{12}N_4$: C, 62.73; H, 4.05. Found: C, 62.32; H, 4.26.

On further recrystallization from the same mixture of solvents the orange prisms were transformed into the yellow needles which melted at 150°, resolidified and finally melted at 183–185°.[25] In U.S.P. chloroform the substance showed a rotation of −69° (*c* 2.6).

Anal. Calcd. for $C_{39}H_{30}O_{12}N_4$: C, 62.73; H, 4.05; N, 7.50. Found: C, 62.90; H, 4.36; N, 7.22.

Acknowledgment.—We wish to thank Dr. W. R. Nes, Mrs. Anne H. Wright, Mrs. Iris J. Siewers and Mrs. Alma J. Hayden for assistance in measuring absorption spectra. Analyses were carried out in the Institute's Microanalytical Laboratory under the direction of Dr. William C. Alford.

BETHESDA, MARYLAND

---

[24] C. Neuberg, A. Grauer and B. V. Pisha, *Anal. Chim. Acta*, **7**, 238 (1952).

[25] Such dimorphism is frequently encountered with 2,4-dinitrophenylhydrazones. See ref. 24.